Supplementary information, Fig. S3. In this figure, cancer cells were treated with DM-αKG (15 mM) for 24 hours to assess DR6 oxidation and pyroptotic features (including morphology, GSDMC cleavage, and LDH release), unless specially indicated otherwise.

(**a**) Inhibitors, Genistein or MβCD, showed no effect on DM-αKG-induced DR6 oxidation. HeLa cells were pretreated with Genistein and MβCD for 2 hours.

(**b**) The knockdown efficiency of CLTA, CLTB, CLAC, DNM1 and DNM2 in HeLa cells as determined by RT-qPCR.

(**c, d, e**) Effect of CLTs on DM-αKG-induced caspase-8 activation (d), pyroptotic morphology (d), GSDMC cleavage and LDH release (e). CLTA, CLTB, and CLAC had first been knocked down in HeLa cells.

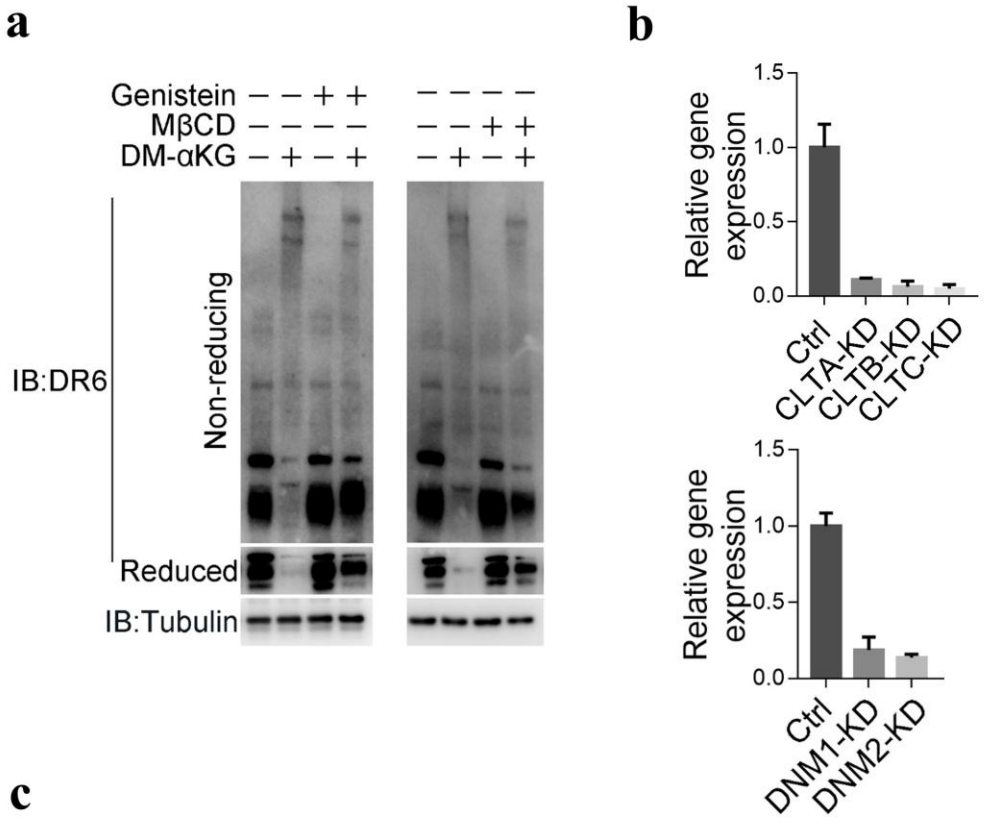
(**f, g, h**) Effect of DNMs on DM-αKG-induced pyroptotic morphology (f), caspase-8 activation (g), GSDMC cleavage and LDH release (h). DNM1 and DNM2 had first been knocked down in the cells.

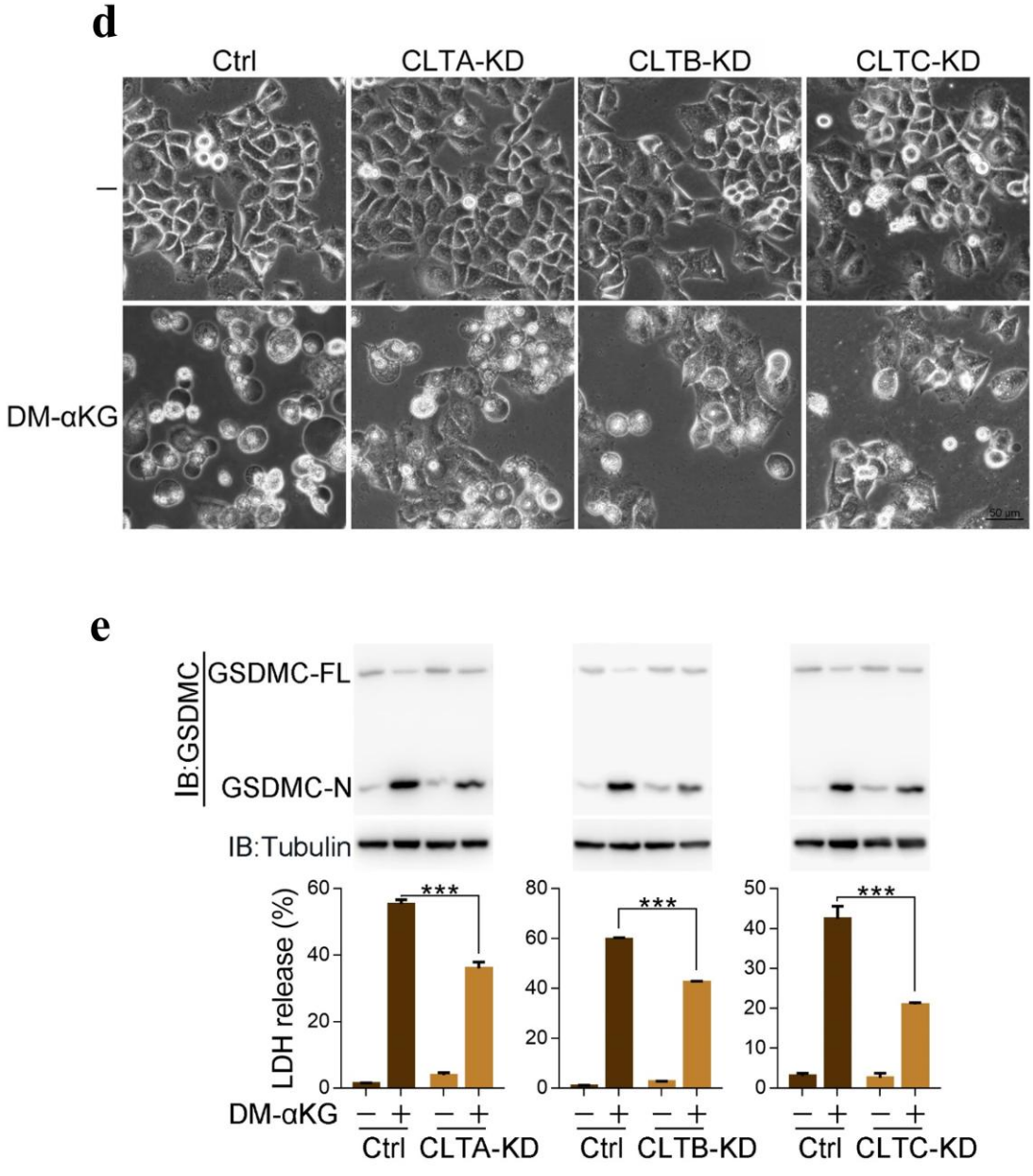
(**i**) Genistein or MβCD impaired DM-αKG-induced GSDMC cleavage in SGC-7901 (top) and B16 (bottom) cells.

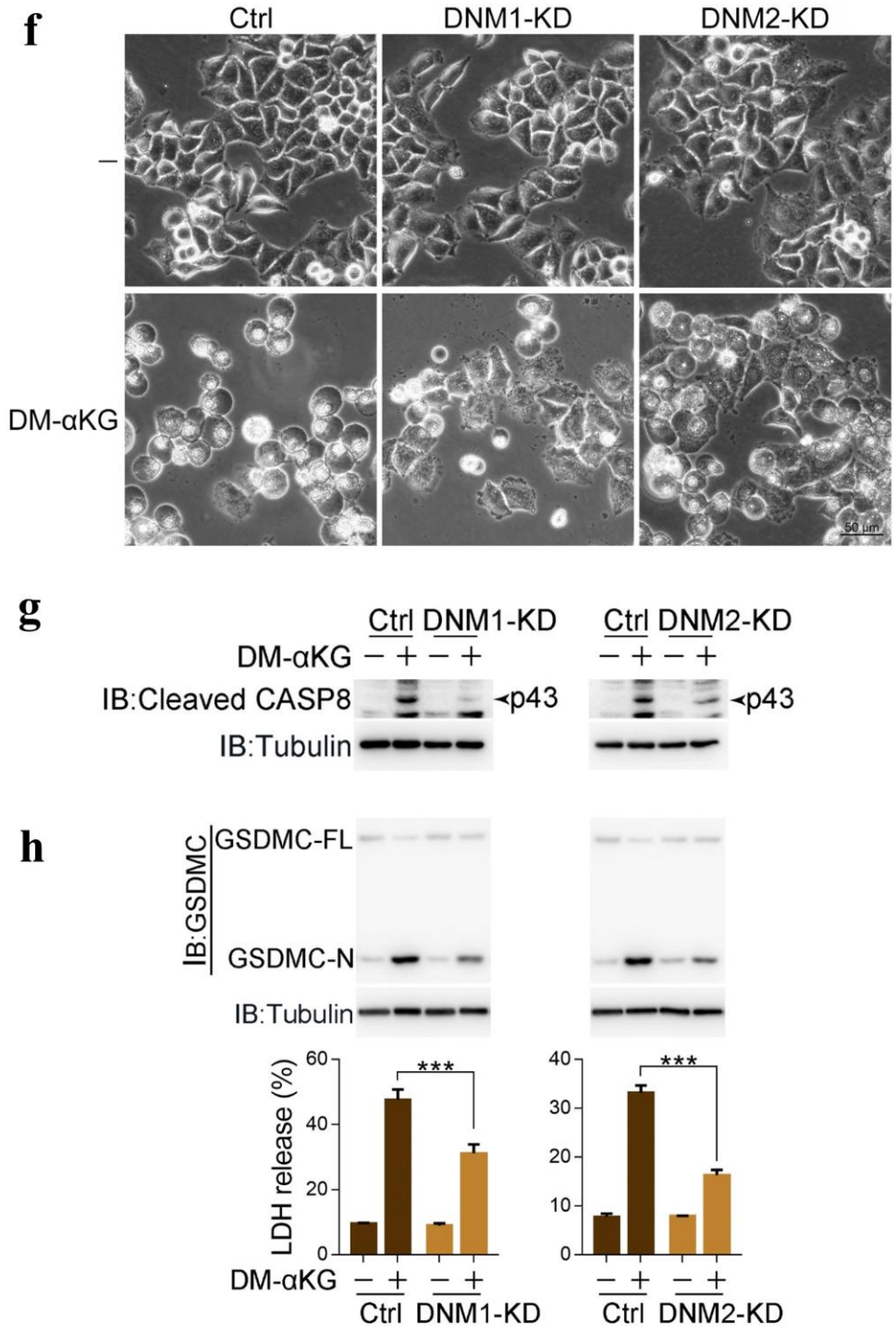
Tubulin was used to determine the amount of loading proteins. All data are presented as the mean±SEM of two or three independent experiments. *** $p<0.001$. The data

were analyzed using two-way ANOVA followed by the Bonferroni test.

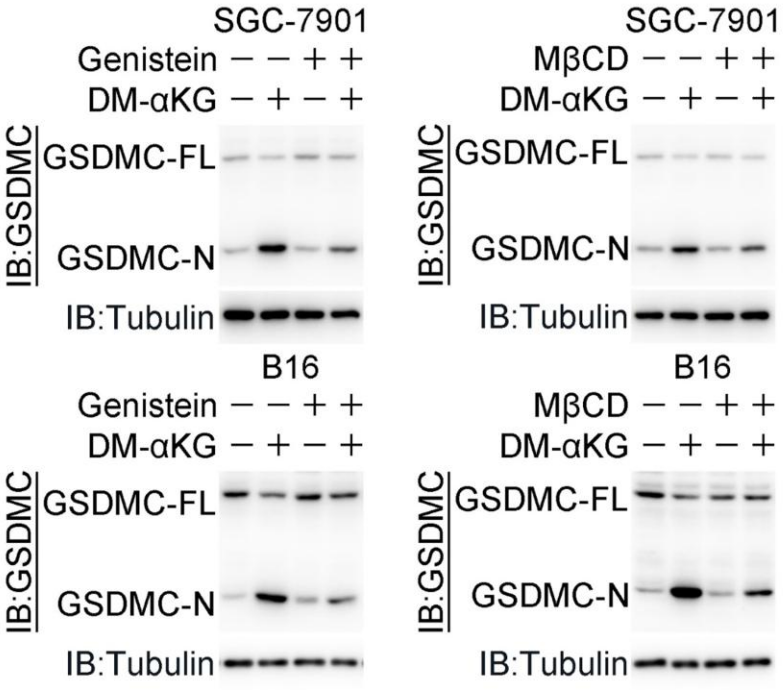
Supplementary information, Figure S3




d
Ctrl
CLTA-KD
CLTB-KD
CLTC-KD
–
DM-αKG
50 μm
e
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin
LDH release (%)
***
DM-αKG
Ctrl
CLTA-KD
CLTB-KD
CLTC-KD


f
Ctrl
DNM1-KD
DNM2-KD
–
DM-αKG
50 μm
g
Ctrl DNM1-KD
Ctrl DNM2-KD
DM-αKG – + – +
– + – +
IB:Cleaved CASP8
p43
p43
IB:Tubulin
h
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin
LDH release (%)
60
40
20
0
***
40
30
20
10
0
***
DM-αKG – + – +
– + – +
Ctrl DNM1-KD
Ctrl DNM2-KD

i


SGC-7901
Genistein − − + +
DM-αKG − + − +
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin
SGC-7901
MβCD − − + +
DM-αKG − + − +
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin
B16
Genistein − − + +
DM-αKG − + − +
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin
B16
MβCD − − + +
DM-αKG − + − +
IB:GSDMC
GSDMC-FL
GSDMC-N
IB:Tubulin